PATENT
Docket No. 313632002300

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Catharina E. HISSINK, *et al.*

Serial No.: 10/586,226

Filing Date: January 14, 2005

For: BIODEGRADABLE MULTI-BLOCK CO-POLYMERS

Confirmation No.: 2740

Group Art Unit: 1762

Examiner: Robert Stockton Jones, Jr.

DECLARATION OF THEODORUS ADRIANUS CORNELIUS FLIPSEN UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Theodorus Adrianus Cornelius Flipsen, declare as follows:

1. I am a co-inventor of the subject matter in the present case. I have worked for InnoCore Technologies since start-up in 2003 and conducted research and development relating to biodegradable multi-block copolymers. In my current position, I am the responsible manager in the Biomaterials Research and Development Group. I have extensive knowledge relating to processes for manufacturing block copolymers and structure-property relationships. I have a Masters degree in Polymer chemistry & physics from The University of Groningen in Groningen, The Netherlands and a Doctorate in Polymer chemistry & physics from the same university. Since 1990 I have

worked in the field of biodegradable polymers in particular multi-block copolymers. Furthermore, I am inventor or co-inventor of various novel polymer systems and polymer applications. A copy of my *curriculum vitae* is attached as Exhibit A.

2. Considering the disclosure in Langer at column 3, lines 7-10 that the phase transition of the hard segment of Langer's materials is at least 10°C higher than that of the soft segment, the interpretation placed on Table 5 of Langer by the Office is in error. When correctly interpreted in light of the above requirement, Table 5 describes polymers with hard segments that melt at a temperature above 37°C, and therefore must necessarily be at least partially crystalline at 37°C.

3. The presence of both a hard and soft segment is seen from the claims of Langer, since claim 1 requires that when the polymers that make up the segments are not blends or crosslinked, as is the case with the polymers in Table 5, the polymers must have a soft and hard segment. That is claim 1 of Langer gives three options for the shape memory materials: the polymer has 1) a hard and a soft segment, 2) at least one soft segment, which is crosslinked covalently or ionically, or 3) polymer blends. As is apparent from the description of the Table 5 polymers in Table 3, both PDL23 and PDL22 have PDS as the hard segment – PDL23 has PLGA as the soft segment and the soft segment of PDL22 is PCL. The segments of the polymers in Table 5 are neither crosslinked, nor do they form a polymer blend. Therefore, in order to be shape memory polymers in accordance with the invention or Langer, these polymers must be in accordance with option 1) and have a hard and a soft segment.

4. The Office states that PDL23 and PDL22 do not show a second melting temperature, and therefore the Tg and Tm shown describe the entire material.

5. In Table 5 PDL23 shows only one phase transition at 34.5°C, which is the Tg of the PLGA segment. PDC22 also shows only one phase transition temperature at 35°C, which is the Tm of the PCL segment. Ttrans of the hard segment is not given, though the presence of a hard segment is required in order for the multi-block copolymers to have a shape-memory character. From this it follows that PDL23 and PDC22 must have a Ttrans of the hard segment of at least 44.5°C and 45°C, respectively, in order to be shape-memory materials, although these values are not shown in Table 5. Since PDS is used as the hard segment in both PDL23 and PDS22, this missing Ttrans must be the melting temperature of the PDS segment. Since both PDL23 and PDS22 both have a melting temperature of the hard segment of at least about 45°C, it follows that these multiblock copolymers are semi-crystalline materials at 37°C as opposed to the completely amorphous materials claimed.

6. I believe that Langer did not purposely omit or report erroneous data, but that the lack of Ttrans in Table 5 of the hard segment is due to the low crystalline content, which apparently could not be measured with the DSC method used. Table 11 shows that PDL23 has shape-memory. It is known that thermal-mechanical testing, as is done for the shape-memory tests, is more sensitive to demonstrate changes in material properties due to phase transitions compared to DSC.

7. In summary, because PDL23 and PDL22 have hard segments with transition temperatures above 37°C, these materials are partially crystalline at this temperature.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that

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such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Groningen, Netherlands, on 5th (day) April (month) 2011.

Theodorus Adrianus Cornelius Filipsen

Curriculum Vitae 2011 - Theo Flipsen, PhD

Personal details:

Last name:	Flipsen
First name:	Theodorus Adrianus Cornelius (Theo)
Date of birth:	March 14, 1968
Nationality:	Netherlands
Telephone:	0031 50 3630777 (PolyVation)
E-mail:	T.Flipsen@polyvation.com

Current employment/work experience

1996 - present

Founder and CEO of **PolyVation BV**

A company for the development and manufacturing of advanced polymer biomaterials.

- Developer of various new polymer biomaterials and healthcare products for customers worldwide
- Website: www.polyvation.com
- At the moment the company employs 18 highly educated persons
- Co-Founder and CEO of two spin-off companies:

- **InGell Labs BV**
  - Founding year: 2010
  - Focus: In situ aqueous gel-forming polymers for injectable drug delivery products
  - Bioresorbable tri-block copolymers end-group modified
  - Bioresorbable graft copolymers
  - Employees: 7
  - Website: www.ingell.nl

- **InnoCore Technologies BV**
  - Founding year: 2004
  - Focus: bioresorbable polymers for parenteral drug delivery products (microspheres, implants and stent coatings)
  - Bioresorbable multi-block copolymers
  - Employees: 15
  - Website: www.innocore.nl

Past employment/work experience

1998 - 2004

Founder and CSO/CEO of **Polyganics BV**

Life sciences company for the development and commercialisation of bioresorbable medical devices for tissue recovery.

- Bioresorbable nerve guides (CE/FDA)
- Bioresorbable nasal dressings (CE/FDA)
- Pipeline with various new products underway
- Bioresorbable nano-segmented lactice/caprolactone copolymers
- Bioresorbable urethane multi-block copolymers
- Bioresorbable phase separated multi-block copolymers
- Employees: 25
- Website: www.polyganics.com

Patents:

1. Maleate-based copolymers and methods for preparing the same: July 2, 2009
2. Dyes and use thereof in ophthalmic lens material: November 3, 2005
3. Biodegradable amorphous multi block co-polyesters: January 12, 2004
4. Biodegradable wound care foams: January 10, 2003
5. Biodegradable drains for medical applications: November 1, 2002
6. Biodegradable phase-separated multi block co-polyesters: July 17, 2002
7. High refractive index flexible silicone: February 8, 2002
8. Biodegradable DL-Lactide-ε-caprolactone copolymers: February 6, 2002
9. Biodegradable intravascular polymeric stent: March 31, 1994

Awards:

2008 Wubbo Ockels Award for inventorship, application and entrepreneurship in the area of material technology. The award is for exceptional performance in technology in relation to the City of Groningen. Wubbo Ockels is the first Dutch astronaut been in space. He studied at the University of Groningen and received the award in 1986, at which the award was given for the first time.

Education:

1992 - 1997 PhD in Polymer Chemistry & Physics
University of Groningen, The Netherlands
Prof. dr. G. Hadziioannou and prof. dr. A.J. Pennings
Subject: "Development of thermally stable polymer optical fibers and polymer optical fiber amplifiers"

1986 - 1992 MSc in Chemistry
University of Groningen, The Netherlands
Specialisation: Polymer chemistry
Thesis laboratory research performed in the group of prof. dr. A.J. Pennings: "Development of a bioresorbable cardio-vascular stent"
Thesis literature research performed in the group of prof. dr. A.J. Pennings: "Biomedical adhesives"

Publications:

1. T.A.C. Flipsen, et.al., Novel biomedical polyurethanes for 'in vivo' tissue regeneration, World Biomaterials Congress, Hawaii, 2000.

2. T.A.C. Flipsen, et.al., A Polymer Optical Fiber with high thermal stability and low optical losses based on novel densely crosslinked polycarbosiloxanes, *Journal of Applied Polymer Science*, **67**, 2223 (1998).

3. T.A.C. Flipsen, et.al., Densely crosslinked polycarbosiloxanes, II: Thermal and Mechanical properties, *Journal of Polymer Science, Part B: Polymer Physics*, **35**, 1311 (1997).

4. T.A.C. Flipsen, et.al., Densely crosslinked polycarbosiloxanes, I: Synthesis, *Journal of Polymer Science, Part A: Polymer Chemistry*, **35**, 41 (1997).

5. Theo A.C. Flipsen, et.al., A novel thermoset polymer optical fiber, *Advanced Materials*, **8**, 45 (1996).